

### REMARKS

Claims 33-53 were pending in the present application. Claims 46-52 were withdrawn from consideration. Claims 33-45 and 53 were rejected. Claims 33, 42 and 45 have been amended. Claims 40, 41, 43, 46, and 50-52, have been canceled. New Claims 54 to 59 have been added. Presently, Claims 33-39, 42, 44-45, 47-49, and 53-59 are pending in the application, and Claims 33-39, 42, 44-45, and 53-59 remain under examination in the present application.

#### Amendments to the Claims are Fully Supported by the Specification as Filed

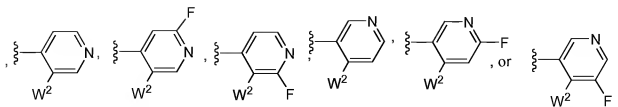
Claim 33 has been amended to define  $W^3$  as  $-O-$  and to define  $W^4$  as  $-CH_2-$ , and to incorporate the definition of  $Y^1$ ,  $Y^2$ ,  $Y^3$  and  $Y^4$  from Claim 40, and the definition of Ar from Claim 43. The definition of CY has been amended to reflect the CY groups exemplified in the present application, particularly, a cyclopentane ring (Examples 11, 13, 20, 73), a pyrrolidine ring (Examples 1,3-7, 9, 22, 23, 30-42, 67-70, 77-81), a piperazine ring (Examples 27, 72), a piperidine ring (Example 8) a benzene ring (Examples 2, 19, 21, 50, 53-55, 64, 66, 89), a pyridine ring (Examples 16, 17, 29, 48, 49, 51, 52, 61, 63, 65, 71, 74, 83, 84, 86-88), a pyrazine ring (Example 85), a pyrrole ring (Examples 12, 56, 57, 59), a pyrazole ring (Examples 14, and 58), an imidazole ring (Examples 24-26, 43-45), a triazole ring (Examples 18, 47), a tetrazole ring (Example 28), an oxazolidine ring (Examples 10, 62), or a thiazole ring (Example 82); which are optionally substituted with two or more substituents selected from Group  $\alpha$ . This definition is also supported by Claim 41.

Claims 40, 41, and 43 have been canceled.

Claim 42 has been amended to delete elements from the Markush group for CY and to change "and pharmaceutically acceptable salts" to "or a pharmaceutically acceptable salt."

Claim 45 has been amended to delete compounds.

New Claims 54 to 59 have been added to more particularly point out and claim specific aspects of Applicants' invention. New Claim 54 depends from base Claim 33, and specifies that  $R^6$  is hydrogen and that  $Y^1$ , and  $Y^4$  are each independently selected from:  $-CH-$ , and  $-CF-$ , and  $Y^2$  and  $Y^3$  are each independently selected from  $-CH-$ ,  $-CF-$ , and  $-N-$ . New Claim 55 depends from Claim 54 and further specifies that  $Y^1$  and  $Y^4$  are each independently selected from:  $-CH-$ , and  $-CF-$ , one of  $Y^2$  and  $Y^3$  is  $-N-$  and the other is selected from  $-CH-$  and  $-CF-$ . New Claim 56 depends from Claim 55 and specifies that CY is as defined in Claim 42, Ar is as defined in Claim 44, and  $Y^1$ ,  $Y^2$ ,  $Y^3$ , and  $Y^4$  together form particular nitrogen-containing six-membered ring structures. Claim 57 depends from Claim 56 and specifies that  $Y^1$ ,  $Y^2$ ,  $Y^3$ , and  $Y^4$  together form:



New Claim 58 depends from Claim 47 and is directed to the compounds of Examples 35, 36, 38, 45-59, 65, 66, 71, and 87-89. New Claim 59 depends from Claim 54 and specifies that CY is as defined in Claim 42, Ar is as defined in Claim 44, and Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup>, and Y<sup>4</sup> are each independently selected from: -CH- and -CF-.

The amendments above are fully supported by the application as filed and do not add new matter to the present application.

#### Entitlement to February 10, 2003 Priority of JP 2003-032123

On May 20, 2009, a certified copy and a certified translation of the foreign priority document of the present application, JP 2003-032123 was transmitted to the USPTO by Express Mail. Applicants respectfully submit that this transmission should perfect Applicants' claim to priority of February 10, 2003. The current claim set is supported by the priority document. References to paragraph numbers below refer to the numbers in the verified translation of JP 2003-032123.

Particularly, Claim 33 finds support in the priority document in priority Claims 1, 2, 10, 11, 13, 17, 18, and in the translated priority specification at paragraphs [0015], [0016], [0062], [0063], [0066], [0070], [0074], [0079], [0083], [0091], [0095], [0099]. Claims 34, 35, 36, 37, 38, 39, 42, and 44 find support in priority Claims 4, 5, 6, 7, 8, 23, 12, and 14, respectively, and in paragraph [0103].

Still further, in Claim 45, the presently claimed compounds find priority in the following examples in JP 2003-032123:

Compound	Priority Document Example No.
2-(3,4-difluorophenyl)-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[5-fluoroisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	6
2-(3,4-difluorophenyl)-N-methyl-2-(1H-1,2,3-triazol-1-yl)-N-[3-(spiro[isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	18
2-(3,4-difluorophenyl)-N-methyl-2-(2H-1,2,3,4-tetrazol-2-yl)-N-[3-(spiro[isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	28
2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1(2H)pyridinyl)-N-[3-	29

(spiro[isobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	
2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[5-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]-acetamide	33
2-(3,4-difluorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1-yl)-N-[3-(spiro[6-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]-acetamide	43
2-(3,4-difluorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1-yl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide	45
2,2-bis(6-fluoro-3-pyridinyl)-N-methyl-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide	48
2-(3,4-difluorophenyl)-N-ethyl-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[isobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide	62
2-(3,4-difluorophenyl)-N-ethyl-2-(4-methanesulfonyl)-2-oxo-1-piperazinyl)-N-[3-(spiro[6-fluoroisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide	67

Claims 47 and 48 are supported by Claims 1 and 15 of the priority document, respectively, and paragraph [0013]. Claim 49 is supported by paragraph [0159]. Claim 53 is supported by Claim 31 of the priority document.

New Claim 54 finds support in the priority document in the original Claim set and specification, as well as in Examples 1, 3, 4, 6, 8-30, 32-36, 38, 43-54, 57, 58, 60-62, 64-66, 67-80, 82 and 83. New Claim 55 finds support in priority document Examples 35, 36, 38, 45-54, 60, 61, 66, 82, and 83. New Claims 56 and 57 find support in paragraphs [0092] and [0093], respectively.

The following the compounds of Claim 58 are specifically exemplified in the Examples of the priority document.

Compound	Priority Document Example No.
2-(4-fluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	35
2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	36
2-(3,4-difluorophenyl)-N-methyl-2-(2-oxo-1-pyrrolidinyl)-N-[3-(spiro[6-fluoro-5-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)-propyl]acetamide	38
2-(3,4-difluorophenyl)-N-methyl-2-(2-methyl-1H-imidazol-1-yl)-N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)-propyl]acetamide	45

2-(3,4-difluorophenyl)-2,2-dimethyl-N-methyl-N-[3-(spiro[5- fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	46
2-(3,4-difluorophenyl)-N-methyl-2-(1H-1,2,4-triazol-1-yl)-N- [3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	47
2,2-bis(6-fluoro-3-pyridinyl)-N-methyl-N- [3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	48
N-methyl-2,2-bis(6-methoxy-3-pyridinyl)-N-[3-(spiro[5-fluoro- 6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	49
2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3- (spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	50
2-(6-fluoro-3-pyridinyl)-N-methyl-2-(6-trifluoromethyl-3- pyridinyl)-N-[3-(spiro[5- fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	51
2-(6-fluoro-3-pyridinyl)-2-(6-methoxy-3-pyridinyl)-N-methyl- N-[3-(spiro[5-fluoro-6-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)- propyl]acetamide	52
2-(6-fluoro-3-pyridinyl)-2-(4-toluy1)-N-methyl-N- [3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	53
2-(6-fluoro-3-pyridinyl)-N-methyl-2-phenyl-N- [3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	54
2,2-bis(4-fluorophenyl)-N-methyl-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	
2-(3,4-difluorophenyl)-N-methyl-2-(1H-pyrrol-1-yl)-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	
2-(4-fluorophenyl)-N-methyl-2-(1H-pyrrol-1-yl)-N-[3-(spiro[5- fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	
2-(3,4-difluorophenyl)-N-methyl-2-(1H-pyrazol-1-yl)-N-[3- (spiro[5-fluoro-6- azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]- acetamide	
2-(3,4-difluorophenyl)-N-methyl-2-(1H)-pyrrol-1-yl)-N-[3- (spiro[6-fluoro-5- azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]- acetamide	
2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3 - (spiro[6-fluoro-5- azaisobenzofuran-1(3H),4-piperidin]-1-yl)propyl]- acetamide	60
2-(6-fluoro-3-pyridinyl)-2-(4-fluorophenyl)-N-methyl-N-[3- (spiro[6- azaisobenzofuran-1(3H),4-piperidin]-1-yl)propyl]acetamide	61
2,2-bis(6-fluoro-3-pyridinyl)-N-ethyl-N-[3-(spiro[5-fluoro-6- azaisobenzofuran-	66

1(3H), 4'-piperidin]-1-yl)-propyl]acetamide	
2-(6-fluoro-3-pyridinyl)-2-(2,4-difluorophenyl)-2-hydroxy-N- methyl-N-[3-(spiro[6-fluoro-5-azaisobenzofuran-1(3H),4'-piperidin]-1-yl)propyl]acetamide	82
2-(2,4-difluorophenyl)-2-(6-fluoro-3-pyridinyl)-2-hydroxy-N- methyl-N-[3-(spiro[6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	83
2,2-bis(4-fluorophenyl)-2-hydroxy-N-methyl-N-[3-(spiro[5- fluoro-6-azaisobenzofuran-1(3H), 4'-piperidin]-1-yl)propyl]acetamide	

New Claim 59 finds support in the claim set as well as in Examples 1, 3, 4, 6, 8-30, 32-34, 43, 44, 57, 58, 62, 64, 65, and 67-80 of the priority document.

35 U.S.C. § 112, second paragraph

The Examiner stated that Claim 1 was rejected under 35 U.S.C. § 112, second paragraph, because of confusing definitions within the Markush elements.

Applicants have previously canceled Claim 1, and have presently amended new base Claim 33 to define W<sup>3</sup> as -O- and W<sup>4</sup> as -CH<sub>2</sub>-, to incorporate the definition of Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup> and Y<sup>4</sup> from Claim 40, the definition of Ar from Claim 43, and a definition of CY that is supported by the Examples and the specification as filed. In so doing, it is believed that the definitions of the Markush groups have been clarified.

In view of the amendments and the remarks above, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 112, first paragraph

Claims 33 to 44, presently Claims 33-39, 42, 44, 53-57 and 59, were rejected under 35 U.S.C. § 112, first paragraph, because the Examiner stated that the specification was not enabling for the full breadth of compounds claimed in the specification. In particular, the Examiner noted that the definition of Ar, CY and Y<sup>1</sup>-Y<sup>4</sup> were broader than the compounds made in the specification.

Applicants have amended base Claim 33, from which Claims 34-39, 42, 44, 53-57 and 59 directly or indirectly depend, to define W<sup>3</sup> as -O- and W<sup>4</sup> as -CH<sub>2</sub>-, to incorporate the definition of Y<sup>1</sup>, Y<sup>2</sup>, Y<sup>3</sup> and Y<sup>4</sup> from Claim 40, the definition of Ar from Claim 43, and have amended the definition of CY to reflect the CY groups exemplified in the present application, particularly, a cyclopentane ring (Examples 11, 13, 20, 73), a pyrrolidine ring (Examples 1,3-7, 9, 22, 23, 30-42, 67-70, 77-81), a piperazine ring (Examples 27, 72), a piperidine ring (Example 8) a benzene ring (Examples 2, 19, 21, 50, 53-55, 64, 66, 89), a pyridine ring (Examples 16, 17, 29, 48, 49, 51, 52, 61, 63, 65, 71, 74, 83, 84,

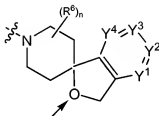
86-88), a pyrazine ring (Example 85), a pyrrole ring (Examples 12, 56, 57, 59), a pyrazole ring (Examples 14, and 58), an imidazole ring (Examples 24-26, 43- 45), a triazole ring (Examples 18, 47), a tetrazole ring (Example 28), an oxazolidine ring (Examples 10, 62), or a thiazole ring (Example 82); which are optionally substituted with two or more substituents selected from Group  $\alpha$ .

Applicants respectfully submit that how to make and use the compounds of the present claims is detailed in the specification with sufficient detail to enable one of ordinary skill in the art to make and use the present invention, and respectfully request reconsideration and withdrawal of the rejection of Claims 33-44, presently Claims 33-39, 42, 44, 53-57, and 59, under 35 U.S.C. § 112, first paragraph.

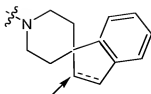
35 U.S.C. § 102(e)

Claims 33-44 and 53, presently Claims 33-39, 42, 44, 53-57, and 59, were rejected under 35 U.S.C. § 102(e) as being anticipated by Marzabadi et al, WO 2004/004714, which the Examiner asserted has an effective filing date of July 3, 2002. The present application has a filing date of February 10, 2003.

Applicants respectfully traverse the rejection of Claims 33-44 and 53, presently Claims 33-39, 42, 44, 53-57, and 59, under 35 U.S.C. § 102(e) as anticipated by Marzabadi WO 2004/004714. As amended, Claim 33, and Claims 34-39, 42, 44, 53-57, and 59 dependent thereon, are directed to compounds with a spiro-isobenzofuran or aza-spiroisobenzofuran moiety at the 4 position of the piperidine group.



Marzabadi WO 2004/004714 was afforded the priority of July 3, 2002, based on the filing of USSN 10/189,146. A copy of 10/189,146 is provided with the Information Disclosure Statement submitted herewith for the convenience of the Examiner. USSN 10/189,146 discloses only carbocyclic rings spiro to the piperidine, e.g.,:



wherein the dotted line represents an optional double bond, and does not disclose any compounds wherein the atom corresponding to  $W^3$  of the presently claimed invention is oxygen. Thus, compounds with a spiro-furan ring were not contemplated in the Marzabadi priority document. The effective date of the Marzabadi WO 2004/004714 reference for any compounds with a spiro-isobenzofuran moiety is July 3, 2003, which is after the February 10, 2003, filing date of the present application.

Still further, Claims 55-57 are directed to compounds wherein one of  $Y^2$  and  $Y^3$  is nitrogen. These aza-spiroazabenzofuran containing structures are not even contemplated by Marzabadi even in the later July 3, 2003, filing of WO 2004/004714.

In view of the amendments and the remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 33-44 and 53, presently Claims 33-39, 42, 44, 53-57, and 59, under 35 U.S.C. § 102(e) as being anticipated by Marzibaldi et al., WO 2004/004714.

#### 35 U.S.C. § 103(a)

Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, 53-59, were rejected under 35 U.S.C. § 103(a) as being unpatentable over Marzabadi et al., WO 2004/004714. The Examiner noted that the compounds of pages 101 to 109, table 1 and Claims 1-28, the process page 45, Scheme E and specific process of making examples of pages 101 to 109 were anticipatory and that the species of present Claim 45 differ only from the prior art compounds only in the substituents on the phenyl rings.

Applicants respectfully traverse the rejection of Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, 53-59, under 35 U.S.C. § 103(a) over Marzabadi, WO 2004/004714. As noted above, the effective date of the Marzabadi WO 2004/004714 reference for any compounds with a spiro-isobenzofuran moiety is July 3, 2003, which is after the February 10, 2003, filing date of the present application. There is not teaching, suggestion, or motivation in the Marzabadi priority document to change the carbocyclic ring structure to the spiro-isobenzofuran and aza-spiroisobenzofuran ring systems where  $W^3$  is -O- of the presently-claimed invention. Still further, Claims 55-58 are directed to compounds wherein one of  $Y^2$  and  $Y^3$  is nitrogen. These aza-spiroazabenzofuran containing compounds are not even contemplated by Marzabadi even in the later July 3, 2003, filing of WO 2004/004714.

In view of the amendments and remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, and 53-59, under 35 U.S.C. § 103(a) over Marzabadi, WO 2004/004714.

#### 35 U.S.C. § 102(g)

The Examiner rejected Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, and 53-59, under 35 U.S.C. § 102(g) as being anticipated by US 2006/0173027. The Examiner pointed to Claims 1-28 of the '027 reference and the present claims drawn to spiroisofuranpiperidines.

Applicants respectfully traverse the rejection of Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, and 53-59, under 35 U.S.C. § 102(g) as being anticipated by US 2006/0173027. US 2006/0173027 is the national phase application of the Marzabadi PCT application which published as WO 2004/004714. As noted *supra*, the Marzabadi priority document USSN 10/189146 does not provide support for the spiro-isobenzofuran and aza-spiroisobenzofuran ring systems where W<sup>3</sup> is -O- of the presently-claimed invention. The spiro-isobenzofuran compounds of US 2006/0173027 claim priority to the CIP filing date, July 3, 2003, which is after the present filing date. Applicants respectfully submit that US 2006/0173027 is not a patent published under section 122(b) filed before the invention by the applicant of the present patent application, because Applicants filing date is prior to the effective filing date of US 2006/0173027 with respect to the spiro-isobenzofuran and aza-spiroisobenzofuran ring systems.

Still further, US 2006/0173027 as published, with its effective filing date of July 3, 2003, does not describe the invention of Claims 55-58, which are directed to compounds wherein one of Y<sup>2</sup> and Y<sup>3</sup> is nitrogen, nor the invention of Claims 33-45, 53, and 54 which read on compounds wherein one of the "Y" groups is nitrogen.

In view of the amendments and remarks above, Applicants respectfully request reconsideration and withdrawal of the rejection of Claims 33-45, and 53, presently Claims 33-39, 42, 44, 45, and 53-59, under 35 U.S.C. § 102(g) as being anticipated by US 2006/0173027.

#### Conclusion

In light of the amendments and remarks above, Applicants believe that the present application is in condition for allowance.



Respectfully submitted,

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